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EXAMINER: **Deborah A. DAVIS**
ART UNIT: **1641**
APPLICANT(S): **H. Garrett WADA et al.**
APPLICATION NO.: **10/613,220**
FILING DATE: **7/2/2003**
ATTORNEY DOCKET NO.: **100/07211**
TOTAL PAGES (incl. Certificate): **11**
DOCUMENT(S): **Transmittal Form; Appellants' Reply Brief Under 37 CFR § 41.41**



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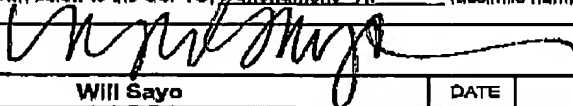
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TRANSMITTAL FORM <small>(to be used for all correspondence after initial filing)</small>	APPLICATION NUMBER	10/613,220	
	FILING DATE	7/2/2003	
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	ART UNIT	1641	
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Appln. No.	:	10/613,220	Confirmation No.:	7051
Applicants	:	H. Garrett Wada et al.		
Filed	:	07/02/2003		
TC/A.U.	:	1641		
Examiner	:	Deborah A. Davis		
Docket No.	:	100/07211		
Customer No.	:	021569		
Title	:	Microfluidic Analytic Detection Assays, Devices, and Integrated Systems		

Commissioner for Patents
P.O. Box 1450
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Appellants' Reply Brief Under 37 CFR §41.41

Sir:

Appellants maintain their appeal and reply to the Examiner's Response, mailed December 01, 2006, in this Reply Brief.

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I. STATUS OF CLAIMS:

Claims 1-23 are pending in the application. Claims 1-23 have been rejected. The rejection of each of claims 1-23 is at issue in this appeal.

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II. GROUND OF REJECTION TO BE REVIEWED ON APPEAL:

Applicants respectfully request that the following grounds of rejection be reviewed on appeal:

Claims 1-23 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nelson et al. US 6,007,690 ("Nelson") in view of Spence et al. US 6,540,895 ("Spence").

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III. ARGUMENT:

Claims 1-23 were rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Nelson in view of Spence. "The examiner bears the initial burden of factually supporting any *prima facie* conclusion of obviousness." See MPEP § 2142. To establish a *prima facie* case of obviousness, three basic criteria must be met: the prior art references must teach or suggest all the claim limitations; there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings; and there must be a reasonable expectation of success. See MPEP § 2143.

At a minimum, the Examiner has not shown that the combination of Nelson and Spence teaches or suggests all of the elements included in Applicants' microfluidic device, element (i) within claim 1, nor has the Examiner shown that the combination teaches "a detection system which is configured to be positioned proximal to the first *and* the second detection regions" (emphasis added).

In the Examiner's Answer mailed December 01, 2006, the Examiner presents a new argument beginning on page 5 of the Answer that is intended to show that all of the limitations of claim 1 are taught by the combination of Nelson and Spence. This new argument cites Figure 16 of Nelson and alleges that Nelson's main electrophoretic flowpath 238 corresponds to Applicants' first microscale channel, and Nelson's "line that connect in-between affinity zone 244 and 246" corresponds to Applicants' second microscale channel. Applicants have interpreted the quoted text as intending to include at least one of affinity zones 244 and 246 in the channel alleged to correspond to Applicants' second microscale channel because the channel ("line") *between* affinity zones 244 and 246 clearly does not and cannot correspond to Applicants' second microscale channel. The Examiner goes on to state, "Each of the affinity zones has detectors (i.e. detection regions) and each affinity zone has enrichment medium that comprise of oligonucleotides immobilized to beads that will become bound and therefore retained within the detection region to a complementary target (i.e. particle stacking zone)."

Thus, the Examiner has specifically named structures in Nelson's Figure 16 that are alleged to correspond to Applicants' first microscale channel, second microscale channel, and

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particle stacking zone. The Examiner has *not* identified any detection region within the first microscale channel and has not specified a detection region in Figure 16 that is alleged to correspond to Applicants' second detection region. The Examiner has not indicated which of the detectors illustrated in Figure 16 (seen at 243, 245, 247, and 249) is/are alleged to correspond to Applicants' detection system. The Examiner has not clearly indicated a structure that is alleged to correspond to Applicants' binding region, though the cited "enrichment medium that comprise of oligonucleotides immobilized to beads that will become bound" may have been intended to suggest a binding region. The Examiner has not identified any "*source* of a component-binding moiety fluidly coupled to the binding region which is capable of binding to the component of interest" (emphasis added).

Applicants will show below, in the discussion regarding Applicants' claimed detection system, that Nelson does not teach a "first detection region" within a "first microscale channel." Because Applicants do not understand the Examiners' intentions with regard to a structure in Figure 16 that allegedly corresponds to Applicants' binding region, this issue will be only peripherally addressed. Therefore, Applicants begin their argument by showing that the Examiner has not identified a *source* of a component-binding moiety fluidly coupled to a binding region because no such source exists in Figure 16.

"All words in a claim must be considered in judging the patentability of that claim against the prior art." *In re Wilson*, 424 F.2d 1382, 1385, 165 USPQ 494, 496 (CCPA 1970). The word "source" has not been considered by the Examiner. A "source" that is "fluidly coupled" to a specified region is not *within* the specified region, but is *separate* from the region and available to the region. Nowhere in Figure 16 is a "source" of a component-binding moiety shown. The oligonucleotide probes of Nelson (column 17, line 21) may represent component-binding moieties, but these probes are "immobilized" (also column 17, line 21) in the enrichment medium and so cannot be a "source of a component-binding moiety fluidly coupled to the binding region." Applicants are unable to identify any structure taught by Nelson that corresponds to Applicants' claimed "source of a component-binding moiety fluidly coupled to the binding region." Thus, Nelson does not teach all of the limitations of the microfluidic device recited within independent claim 1. Spence is silent with regard to a channel comprising a gel

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filled component separation region and so cannot teach a source of a component-binding moiety fluidly coupled to a binding region that is fluidly coupled to or within such a channel.

Further, the references cited by the Examiner neither teach nor suggest a detection system configured to be positioned proximal to *both* a first detection region in a microscale channel comprising a gel filled component separation *and* a second detection region in a microscale channel configured to contain a particle set therein. The following argument also shows that neither Nelson nor Spence teaches detection regions positioned within *both* a first microscale channel comprising a gel filled component separation *and* a second microscale channel configured to contain a particle set therein.

Figure 16 of Nelson (described in column 17, lines 9–41) shows four separate detectors 243, 245, 247, and 249, each detector associated with a single affinity zone. Affinity zones 244, 246, 248, and 250 function as enrichment channels in this embodiment, with the affinity zones capturing different target DNA fragments. As no detector is associated with main electrophoretic flowpath 238 in Figure 16, it is clear from the figure and the text that main electrophoretic flowpath 238 does not include a detection region.

While other figures of Nelson, for example Figures 18 and 19, show a detection region within a separation channel, nothing in Nelson teaches or suggests a system having detection regions within *both* a channel comprising a separation region *and* a channel configured to contain a particle set.

The problem to be solved by Nelson is detecting low-concentration analytes, particularly in a system that includes electrophoretic separation of a sample. "Because of the nature of the electrophoretic chambers employed in CE [capillary electrophoresis] and MCE [microchannel electrophoresis], good results are not generally obtainable with samples having analyte concentrations of less than about 10^{-6} M." Column 1, lines 34–37. "Accordingly, there is continued interest in the development of improved CE devices capable of providing good results with samples having low concentrations of analyte, particularly analyte concentrations in the femtomolar to nanomolar range." Column 2, lines 17–21.

In nearly all of the embodiments taught by Nelson, an enrichment channel precedes the electrophoretic flowpath. This configuration is shown, for example, in Figures 18 and 19. (Please note that Applicants have demonstrated in their Appeal Brief that these figures

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neither teach nor suggest all the limitations of Applicants' claim 1.) In these embodiments, the enriched and electrophoretically separated analyte is detected in, or downstream of, the electrophoretic flowpath. The low-concentration analyte can be detected at this point because it has been not only enriched in the enrichment channel, but also separated. No purpose would be served by positioning a detection system proximal to the jumble of analytes present in the enrichment channel prior to separation. Thus, Nelson neither teaches nor suggests positioning a detection system proximal to *both* the electrophoretic flowpath *and* the enrichment channel where the enrichment channel precedes the electrophoretic flowpath. By the same token, Nelson neither teaches nor suggests including a detection zone in both the electrophoretic flowpath and the enrichment channel where the enrichment channel precedes the electrophoretic flowpath.

In Figure 16, cited in the Examiner's Answer, the electrophoretic flowpath precedes a series of enrichment channels. As previously discussed, affinity zones 244, 246, 248, and 250 function as enrichment channels in this embodiment, with the affinity zones capturing different target DNA fragments. While it is not clear to Applicants what benefit is derived from separating the sample prior to introducing it into the serial array of affinity zones (each of which has its own associated detector), it is quite apparent that no purpose can be served by attempting to detect a low-concentration analyte in the electrophoretic flowpath prior to enrichment. Thus, Nelson neither teaches nor suggests positioning a detection system proximal to *both* main electrophoretic flowpath 238 (alleged by the Examiner to correspond to Applicants' first microscale channel) *and* a channel that extends through affinity zones 244 and/or 246 (alleged by the Examiner to correspond to Applicants' second microscale channel). By extension, Nelson neither teaches nor suggests including a detection zone in both the electrophoretic flowpath and the enrichment channel where the electrophoretic flowpath precedes the enrichment channel.

Spence does not teach either a first microscale channel comprising a gel filled component separation region or a second microscale channel configured to contain a particle set. Therefore, Spence cannot teach detection regions within such channels or a detection system configured to be positioned proximal to such detection regions.

Thus, the combination of Nelson and Spence neither teaches nor suggests all of the claim limitations of Applicants' independent claim 1. Further, Applicants respectfully assert

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that the Examiner has not demonstrated either a suggestion or motivation to combine the teachings of Nelson and Spence.

"In determining the differences between the prior art and the claims, the question under 35 U.S.C. 103 is not whether the differences themselves would have been obvious, but whether the claimed invention as a whole would have been obvious." See MPEP §2141.02(I). In claim 1, Applicants claim a system that comprises a separation channel upstream from a channel configured to contain a particle set (a "particle channel"). Each of these channels includes a detection region, and both of these channels are proximal to a detection system. Thus, Applicants' claimed system provides detectable results from both the separation channel and the "particle channel." As previously discussed, Nelson teaches a system for detecting low-concentration analytes that includes electrophoretic separation of a sample. The emphasized utility of the apparently preferred embodiments of Nelson's invention is that "waste fluid from the enrichment channel [particle channel] does not flow through the main electrophoretic channel [separation channel]." See column 4, lines 8-10. Spence teaches a microfabricated device for sorting cells. A person of skill in the art would not be motivated to combine a system for detecting low-concentration analytes following enrichment with a device for sorting cells to produce Applicants' claimed invention taken as a whole.

The Examiner asserts on page 6 of the Answer that systems of Nelson are "configured to perform western and southern blot analysis." Nelson states, "The configuration of FIG. 19 can be used, for example, for a flow-through analysis analogous to a Southern blot analysis." See column 18, lines 45-47. Nelson does not claim that *any* configuration illustrated can be used to perform western blot analysis. As Applicants have demonstrated in their Appeal Brief, the system of Figure 19 of Nelson is quite different from Applicants' claimed system and does not teach every limitation of Applicants' claim 1. Therefore, the fact that the system of Figure 19 is claimed (but not shown) to perform a Southern blot analysis is irrelevant.

Applicants respectfully submit that the Examiner has not met the initial burden of factually supporting a *prima facie* conclusion of obviousness with regard to Applicants' independent claim 1. As a result, claim 1 is nonobvious. Claims 2-23 depend directly or indirectly from independent claim 1. Any claim depending from a nonobvious claim is also

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nonobvious. See MPEP § 2143.03 and *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). Therefore, dependent claims 2-23 are also allowable over the combined references.

For the foregoing reasons, Appellants maintain that all of the pending claims are allowable over the combined references and respectfully request that the present rejections under 35 U.S.C. § 103(a) be withdrawn.

Respectfully submitted,



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